Phototherapy with UVB narrowband, UVA/UVBnb, and UVA1 differentially impacts serum 25-hydroxyvitamin-D3

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Abstract: BACKGROUND: Ultraviolet (UV) B radiation increases serum 25-hydroxyvitamin-D3 [25(OH)D], but the influence of UVA1 and UVA/narrowband UVB (UVBnb) phototherapy on serum vitamin D is unknown. OBJECTIVE: We sought to investigate the influence of UVBnb, UVA1, and UVA/UVBnb phototherapy on serum levels of 25(OH)D and related parameters in patients with an inflammatory skin condition. METHODS: 25(OH)D, as well as calcium, parathormone, phosphate, and albumin were measured before therapy, 2 weeks after start, and after completion of the phototherapy. Diagnoses were divided in 4 groups: atopic dermatitis, psoriasis, morphea, and others. RESULTS: We surveyed 116 dermatologic patients undergoing phototherapy with UVA1 (n = 38), UVA/UVBnb (n = 30), or UVBnb (n = 48) 2 to 3 times a week for 53 to 90 days. UVBnb phototherapy increased serum 25(OH)D from 22.1 to 39.5 ng/mL after the therapy ($P < .001$). The lower the baseline 25(OH)D level was, the steeper the increase in 25(OH)D was upon application of UVBnb phototherapy. UVA/UVBnb therapy also increased serum 25(OH)D, from 23.9 to 50.3 ng/mL ($P = .003$). Conversely, in the UVA1 therapy group, 25(OH)D serum levels decreased significantly from 21.9 to 19.0 ng/mL ($P < .001$). LIMITATIONS: The study design was open trial without randomization. An influence of a precise skin disease cannot be excluded because of the heterogeneous diagnoses. Bias may have arisen from patient preference for treatment at our center, referral, unrecognized differences in underlying skin disease, and other factors. CONCLUSION: Phototherapy with UVBnb and UVA/UVBnb increased 25(OH)D serum level significantly. UVA1 therapy alone induced a reduction in serum 25(OH)D concentrations.

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Phototherapy with UVB narrowband, UVA/UVBnb and UVA1 differentially impacts serum 25-hydroxyvitamin D

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Key words: vitamin D, phototherapy, ultraviolet A, ultraviolet B, inflammatory skin disease, open observational study

Abbreviations: 25(OH)D: 25-hydroxyvitamin D3; BMI: body mass index DLQI: Dermatology Life Quality Index; UV: ultraviolet light

Capsule summary:

What is already known about this topic

- Ultraviolet (UV) B radiation increases serum 25-hydroxyvitamin-D3

What this article adds to our knowledge

- Phototherapy with UVA/UVBnb increased 25(OH)D serum level significantly
- UVA1 therapy alone induced a reduction in serum 25(OH)D concentrations.

How this information impacts clinical practice and/or changes patient care

- Particular wave-lengths such as UVA1 and presumably also sunbeds which emit mainly UVA may not be helpful for vitamin D synthesis or even be detrimental, thus calling for attention to oral vitamin D supplementation in individuals concerned.

Abstract

Background: Ultraviolet (UV) B radiation increases serum 25-hydroxyvitamin-D3 [25(OH)D], but the influence of UVA1 and UVA/UVBnb phototherapy on serum vitamin D is unknown.

Objective: To investigate the influence of narrowband UVB (UVBnb), UVA1 and UVA/UVBnb phototherapy on serum levels of 25(OH)D and related parameters in patients with an inflammatory skin condition.

Methods: 25(OH)D, as well as calcium, parathormone, phosphate and albumin were measured before therapy, two weeks after start as well as after completion of the phototherapy at week 12. Diagnoses were divided in four groups: atopic dermatitis, psoriasis, morphea and others.

Results: We surveyed 116 dermatological patients undergoing phototherapy with UVA1 (n=38), UVA/UVBnb (n=29) or UVBnb (n=49) two to three times a week for 53-90 days. UVBnb phototherapy increased serum 25(OH)D from 22.1 to 39.5ng/ml after the therapy ($p<0.001$). The lower the baseline 25(OH)D level was, the steeper the increase in 25(OH)D was upon application of UVBnb phototherapy. UVA/UVBnb therapy also increased serum 25(OH)D, from 23.9 to 50.3ng/ml ($p=0.003$). Conversely, in the UVA1 therapy group, 25(OH)D serum levels decreased significantly from 21.9 to 19.0ng/ml ($p<0.001$).

Limitations: The study design: open randomized trial without randomization. An influence of a precise skin disease cannot be excluded because of the heterogeneous diagnoses. Bias may have arisen from patient preference for treatment at our center, from referral, from unrecognized differences in underlying skin disease and other factors.

Conclusion: Phototherapy with UVBnb and UVA/UVBnb increased 25(OH)D serum level significantly. UVA1 therapy alone induced a reduction in serum 25(OH)D concentrations.

INTRODUCTION

Phototherapy with ultraviolet light is a safe and effective treatment for a variety of inflammatory skin diseases. After replacing the broadband UVB (280-320 nm), narrowband UVB (311 nm) has become the first-line phototherapy due to its high efficacy and safety. UVB phototherapy has been shown to increase serum 25(OH) D concentrations in several studies.[1, 2]

In the last decade, ultraviolet A1 (UVA1, 340-400nm) phototherapy has emerged as a therapeutic modality in sclerosing and inflammatory skin conditions, and vitamin D has been identified as important mediator in inflammatory skin disease.[3] No data is available on vitamin D level variations under UVA1 phototherapy. A randomized controlled trial showed a significant increase in 25(OH)D serum levels after use of sunbeds emitting 0.5% and 1.4% UVB.[4] A significant increase in 25(OH)D had also been described after use of UVA sunbeds emitting only 0.36% of UVB.[5]

Although the action spectrum for the conversion of 7-dehydrocholesterol to vitamin D3 is thought to be within the UVB range (280-320 nm), these results suggest that the higher wavelengths of UVA (320-400 nm) may as well have an effect. Nevertheless, the possibility that the small amounts of UVB emitted by these lamps might explain the increase either alone or in combination with UVA has not been ruled out. We investigated the serum levels of 25(OH)D under UVBnb, UVA/UVBnb and UVA1 phototherapy.[6]

MATERIALS AND METHODS

Design

An open observational study was conducted at Zurich University Hospital, Zurich,

Switzerland, from April 2009 to February 2011. The objective was to investigate the influence of UVBnb (311nm), UVA/UVBnb (320-400nm/311nm) and UVA1 (340-400nm) therapy on the serum vitamin D level measured as 25-hydroxyvitamin D3 [25(OH)D]. The Medical Ethics Committee of Zurich approved the study (H-B-2007-100), which was conducted according to the Declaration of Helsinki principles. All participants gave oral and written informed consent.

Patients

Weight and height were recorded and the body mass index (BMI) was calculated. The inclusion criteria were: Adult patients with a skin disease and the dermatological indication for a phototherapy with UVBnb, UVA/UVBnb or UVA1 as well as oral and written informed consent. The phototherapy was chosen according to the skin disease (for example psoriasis is treated with UVBnb, morphoea with UVA1; cf. Table 3). Participants were excluded from for the study if they did not complete the phototherapy, had a break of 2 weeks or more in the phototherapy course, or withdrew their consent to participate (Figure 1). Diagnosis groups were defined as follows: morphea/scleroderma (group 1), atopic dermatitis (group 2), psoriasis (group 3) and other (group 4) (Table 3).

Definition of vitamin D sufficiency

According to the World Health Organization, in this study, vitamin D insufficiency is defined as 25(OH)D level <20 ng/ml (< 50 nmol/L) and vitamin D deficiency as 25(OH)D level <10 ng/ml (< 25 nmol/L).[7]

Statistical considerations and methods

A minimum of 90 patients needed to enter this study. The study was aimed to detect a relationship between the cumulative UV dose and dependent variables at a two-sided

5.000 percent significance level. The true change in the dependent variables is 0.531 standard deviations per one standard deviation change in the cumulative UV dose. Descriptive statistics of all the variables in the dataset were analyzed: mean, standard deviation, median, and IQR for continuous variables and frequencies and relative frequencies for discrete variables.

Associations between two discrete variables were investigated by Chi-Square test. For paired discrete variables the McNemar test was applied. Mann-Whitney test was used in order to disclose differences in means of a continuous variable between two groups. In order to investigate differences in a continuous variable with respect to discrete factor with more than two levels, the one-way ANOVA together with the Scheffé post-hoc test was computed. Possible linear associations between two continuous variables were analyzed by means of the non-parametric Spearman correlation. The influence of time on continuous variables was investigated by the paired t-test. In order to gain the global view of the associations within the data set the multiple linear regression analysis was applied. Data were coded in Excel and analyzed in SPSS version 19. Results of the statistical analysis with p-value smaller than 5 percent were considered to be statistically significant.

Agent doses and administration

Patients enrolled in the study underwent phototherapy with UVBnb, UVA/UVBnb or UVA1 in the physical therapy unit of the Department of Dermatology according to the standard light therapy algorithm. Generally, UVBnb treatment is initiated at 0.1 J/cm^2 per session and is increased in increments of 20% from session to session, provided there are no side effects, such as UV-induced erythema, limiting further dose escalation. The typical maximum dose for UVBnb is 2.0 J/cm^2, but is individually adjusted based on the

clinician's discretion. Typically, three sessions are performed weekly for a maximum of 12 weeks. Generally, UVA1 treatment is initiated after phototesting on a small area and conducted at 50 J/cm^2 per session. The typical maximum dose for UVA1 is 50 J/cm^2 (medium-dose UVA1). Typically, three sessions are performed weekly for a total of 30 sessions resulting in a cumulative dose of 1500 J/cm^2. The UVA/UVBnb treatment protocol consists of parallel application of UVA at a starting dose of 0.5 J/cm2 with increments of 20% increasing to a maximum dose of 5 J/cm2 during the standard UVBnb phototherapy.

Phototherapy was performed with an UVBnb lamp (Waldmann, UV 1000, output 310 - 315 nm, peak 311 nm), an UVA/UVBnb lamp (Waldmann, UV 7002, UVA: output 320 - 410 nm, peak 351 nm; UVB output 310 - 315 nm, peak 311 nm) and a UVA1 lamp (Sellamed 24'000, output 340–420 nm, peak 380 nm). The UV sources irradiated all body surface areas with equal intensity. No radiation in the infrared or UVB region was detectable in the UVA1 lamp.

Clinical evaluation

Clinical examination of the skin was performed on day 0, day 14 and at completion of therapy at about 12 weeks.

Laboratory measurements

Serum 25(OH)D, as well as plasma levels of calcium, parathormone, phosphate, albumin and CRP levels were measured at day 0, day 14 and at completion of therapy at about 12 weeks. Calcium level was corrected with albumin level.

Study completion

A patient was considered to have completed the study after visit 3 and the last blood sampling.

RESULTS

Of 126 screened patients, eight refused to participate or were not included because they could not complete phototherapy in our phototherapy unit. Two were excluded being minors below 18 years of age. We surveyed 116 dermatological patients undergoing phototherapy with UVA1 (n=38), UVA/UVBnb (n=30) or UVBnb (n=48) two to three times a week for 53-90 days. Of 116 participants (54 females and 62 males aged 18-83 years, median age 49.7 years old; women 47.2, men 48.4) entering the study, a total of 84 participants completed the study (Figure 1). Reasons for dropouts were loss to follow-up in 31 patients and exclusion in one patient because phototherapy was changed to PUVA-therapy.

Population parameters before therapy

The age was similar across all therapy groups (p= 0.905). The baseline 25(OH)D level was comparable in all 3 groups before therapy as well as between the different diagnosis groups (p= 0.851).

Influence of phototherapy on 25(OH)D concentrations

Serum levels of 25(OH)D increased under UVBnb therapy, from 22.1 (+/- 10.3) to 39.5 (+/- 12.2) ng/ml (increase 18.6 +/- 4.6 ng/ml; p<0.001). This effect was already detectable after 2 weeks of phototherapy (p<0.001) (Figure 2a, Figure 2b, Table 2). The increase in 25(OH)D level after UVBnb exposure correlated inversely with baseline 25(OH)D level (P<0.001), where the patients with the lowest basal 25(OH)D level showed the most pronounced increase.

UVA/UVBnb therapy increased 25(OH)D from 23.9 (+/- 20.2) to 50.3 (+/- 22.9) ng/ml by week 12 (increase 29.7 +/- 3.7 ng/ml; p=0.003). However, this increase was not significant at 2 weeks (p= 0.157) (Figure 2a, Figure 2b, Table 2). No difference was

detected in the increase of 25(OH)D between UVBnb and UVA/UVBnb phototherapies (p=0.652). In both UVBnb and UVA/UVBnb phototherapies, a relationship between the cumulative UVBnb dose and the increase in vitamin D could not be observed.

On the other hand, under UVA1 therapy, a decrease in the 25(OH)D serum level from 21.9 (+/- 9.7) to 19.0 (+/- 8.3) ng/ml was measured between week 0 and week 12 (decrease -1.1 +/- 3.3 ng/ml; p<0.001; figure 2b). This effect was not detectable yet at 2 weeks (p= 0.217) (Figure 2a). A trend for a relationship between the cumulative UVA1 dose and the vitamin D decrease was observed (p= 0.0983).

Before therapy with UVBnb there were eight insufficient (<20 ng/ml) and five deficient (<10 ng/ml) patients, and only two showed an insufficiency after therapy (no deficiency). In the UVA/UVBnb group, there were five insufficient and four deficient patients before therapy and only one insufficient patient after therapy (no deficient ones), respectively. In the UVA1 group, 14 patients had an insufficient 25(OH)D serum level and one was deficient in 25(OH)D. After UVA1 therapy, we detected 15 insufficient and five deficient patients.

Influence of gender on serum vitamin D level

No gender difference was observed in any single treatment group.

Influence of season on serum vitamin D level

Blood samples taken in winter and spring were grouped together as “winter”(w), in summer and fall grouped together as “summer”(s). Patients were then classified into 4 different groups, depending on when they had the 1st and the 2nd blood sampling (w-w, w-s, s-w, s-s). Before therapy, the vitamin D serum level was significantly lower in the

winter group (p = 0.012, table 1). But the effect of phototherapy was independent of the season: We did not observe a relationship between these 4 groups and the vitamin D serum level (p= 0.125 for UVA1, p= 0.467 for UVA/UVBnb, p= 0.147 for UVBnb, p= 0.150 for all therapy groups together) at the end of therapy.

Influence of phototherapy on the other parameters

The plasma levels of albumin-corrected calcium, phosphate, parathormone and CRP were not influenced by any of the phototherapies. Changes in systolic and diastolic blood pressure were not correlated to 25(OH)D serum level change. BMI, age and diagnosis were neither correlated to serum 25(OH)D change nor to phototherapy used. We did not observe any correlation between age and vitamin D synthesis (p values in Table 1).

Quality of life and phototherapy

DLQI improved in the total patients' collective ($p<0.001$), as well as in each phototherapy group considered separately, however, we could not detect a difference between the phototherapy groups. DLQI did not correlate with the change in the vitamin D serum level.

DISCUSSION

Our study confirms the results of previous studies showing that UVBnb phototherapy increases serum vitamin D levels. In a case series of women with psoriasis, UVB broadband treatment for 8-12 weeks increased serum levels of 25(OH)D 1.62-fold from base level.[8] Almost all studies were performed with UVB broadband and only seven recent studies investigated the plasmatic increase of vitamin D under UVBnb.[9-15] Czarnecki et al. showed that one oral dose of 50'000 IU of cholecalciferol raised the

serum level by 3.5 mmol/l on average, which was similar to the effect of one dose of UVBnb to the entire body surface.[13] Only one study observed a vitamin D increase in the plasma under psoralen-UVA therapy, however the authors could not exclude a role for the small amount of UVB emitted by the lamp.[16]

Our observation that individuals with low initial concentrations of 25(OH)D have a higher response to UVBnb irradiation confirmed previous reports.[4, 11, 17] We did not find any correlation between the cumulative dose of UVBnb and the increase of serum 25(OH)D at 12 weeks, in accordance with Osmancevic et al.[14] but in contradiction to a recent study.[18] The explanation might be that 25(OH)D reaches a plateau after 3 weeks already, and that exposure to additional UVBnb may not result in a continued proportional increase in serum vitamin D.[19]

Importantly, UVBnb as well as UVA/UVBnb therapies increased vitamin D serum levels in most insufficient and deficient individuals to the normal range, whereas therapy with UVA1 slightly reduced the vitamin D serum level, and resulted in an increased number of insufficient and deficient patients. This observed decrease of serum vitamin D after UVA1 phototherapy has not been documented to date. A possible explanation is that vitamin D absorbs UVA1 besides UVBnb and becomes susceptible to degradation.[20] Although the decrease is statistically significant, we cannot conclude that the effect of UVA1 on 25(OH)D is biologically relevant. However, we demonstrate that there is no 25(OH)D increase with this wavelength.

We found that the season when the therapy took place had no significant influence on the vitamin D level increase during UV therapy, both when considering all therapies together and each treatment modality separately. This is comparable to the results from

Lesiak et al., showing that vitamin D serum level changes with UVBnb were related to the season of the irradiation after 10 phototherapy sessions, but not after 20; our data were recorded after 12 weeks of phototherapy, representing about 36 sessions, a duration of such length that we expected no differences.[15]

Our finding that the plasma level of calcium, phosphate, and CRP were not influenced by any of the phototherapies is in accordance to previous studies.[8, 12, 14] The PTH level was inversely correlated to serum 25(OH)D levels, but the PTH level changes were not significant in any of the phototherapy groups. This cannot be explained by an insufficient increase in vitamin D serum level, as most patients that were insufficient or deficient before therapy had vitamin D in the normal range after UVBnb or UVA/UVBnb therapy. Our results are in accordance with the studies of Osmancevic et al., reporting a suppression of PTH along with an increase in vitamin D synthesis under UVBbb and UVBnb therapies but significant only under UVBbb therapy.[8, 12, 14] However we cannot exclude a significant PTH decrease with a greater patient number, as we observe a tendency towards a reduction of plasmatic PTH.

Krause et al. showed that serial whole-body irradiation with an artificial UVB source, in contrast to a UVA source, could reduce blood pressure in patients with untreated mild hypertension.[21] In our study, no change in systolic and diastolic blood pressure could be correlated with 25(OH)D levels, but our population was normotensive. The ability to synthesize vitamin D decreases with age.[22] We were not able to observe any correlation between age and vitamin D synthesis, in line with other previous studies.[8, 12, 21] We observed also no relationship between BMI and vitamin D change, confirming the results of previous studies.[6, 23] Diagnosis was neither correlated to the extent of serum vitamin D change nor to phototherapy modality. It has been shown that the UVBnb course

increases 25(OH)D in the healthy subject similarly to the patients with psoriasis and atopic dermatitis[9], implying that inflamed skin is also able to produce 25(OH)D under the influence of UVBnb.

Missing data hampered the analysis of the quality of life index in our study: complete information (DLQI before and after therapy) was available for 25 patients only. DLQI data was sufficiently complete, however, to document an increase in health related quality of life along phototherapy, while the number of completed questionnaires may limit the observed lack of correlation to serum vitamin D changes.

The strength of our study is the prospective design with standardized treatments and blood analysis. Among the main limitations of the study is the study design: this open randomized trial may be biased compared to a randomized controlled trial. Moreover, the type of phototherapy was chosen according to the dermatological diagnosis, excluding randomization. The different therapy groups are composed of heterogeneous diagnoses, and an influence of a precise skin disease cannot be excluded. Bias may have arisen from patient preference for treatment at our center, from referral, from unrecognized differences in underlying skin disease and other factors. The basal vitamin D level was comparable, independent of the diagnosis, but we cannot rule out a possible effect of different skin diseases on the individual susceptibility to UVA and/or UVB.

In conclusion, phototherapy has an impact on 25(OH)D levels in the serum. UVBnb is a potent inducer of serum 25(OH)D reaching considerable effects already after 2 weeks. Notably, UVA1 therapy led to a decrease in serum 25(OH)D levels, suggesting that wavelength spectrum of photoexposure is important. While phototherapy induced 25(OH)D synthesis irrespective of age, gender, BMI, season of the year or underlying

skin condition, and increases were biologically relevant under UVBnb as well as under UVA/UVBnb, we think that oral supplementation is more appropriate to correct 25(OH)D deficiency and to maintain adequate 25(OH)D levels in order to avoid the pro carcinogenic effect of UVB.[24, 25] Particular wave-lengths such as UVA1 and presumably also sunbeds which emit mainly UVA may not be helpful for vitamin D synthesis or even be detrimental, thus calling for attention to oral vitamin D supplementation in individuals concerned. Our study data calls for closer examination of a potential confounding effect of various skin diseases and of the need for oral vitamin D supplementation in UVA1-treated patients.

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REFERENCES

1. Armas LA, Dowell S, Akhter M, Duthuluru S, Huerter C, Hollis BW et al. Ultraviolet-B radiation increases serum 25-hydroxyvitamin D levels: the effect of UVB dose and skin color. J Am Acad Dermatol 2007;57:588-93.
2. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. Am J Clin Nutr 1999;69:842-56.
3. Chu CC, Ali N, Karagiannis P, Di Meglio P, Skowera A, Napolitano L et al. Resident CD141 (BDCA3)+ dendritic cells in human skin produce IL-10 and induce regulatory T cells that suppress skin inflammation. The Journal of experimental medicine 2012;209:935-45.
4. Thieden E, Jorgensen HL, Jorgensen NR, Philipsen PA , Wulf HC. Sunbed radiation provokes cutaneous vitamin D synthesis in humans--a randomized controlled trial. Photochem Photobiol 2008;84:1487-92.
5. Devgun MS, Johnson BE , Paterson CR. Tanning, protection against sunburn and vitamin D formation with a UV-A 'sun-bed'. Br J Dermatol 1982;107:275-84.
6. Schlumpf M, Reichrath J, Lehmann B, Sigmundsdottir H, Feldmeyer L, Hofbauer GF et al. Fundamental questions to sun protection: A continuous education symposium on vitamin D, immune system and sun protection at the University of Zurich. Dermatoendocrinol 2010;2:19-25.
7. Holick MF. Vitamin D deficiency. The New England journal of medicine 2007;357:266-81.
8. Osmancevic A, Landin-Wilhelmsen K, Larko O, Mellstrom D, Wennberg AM, Hulthen L et al. UVB therapy increases 25(OH) vitamin D syntheses in postmenopausal women with psoriasis. Photodermatol Photoimmunol Photomed 2007;23:172-8.
9. Vahavihu K, Ala-Houhala M, Peric M, Karisola P, Kautiainen H, Hasan T et al. Narrowband ultraviolet B treatment improves vitamin D balance and alters antimicrobial peptide expression in skin lesions of psoriasis and atopic dermatitis. Br J Dermatol 2010;163:321-8.
10. Vahavihu K, Ylianttila L, Kautiainen H, Viljakainen H, Lamberg-Allardt C, Hasan T et al. Narrowband ultraviolet B course improves vitamin D balance in women in winter. Br J Dermatol 2010;162:848-53.
11. Cicarma E, Mork C, Porojnicu AC, Juzeniene A, Tam TT, Dahlback A et al. Influence of narrowband UVB phototherapy on vitamin D and folate status. Exp Dermatol 2010;19:e67-72.
12. Osmancevic A, Landin-Wilhelmsen K, Larko O, Wennberg AM , Krogstad AL. Vitamin D production in psoriasis patients increases less with narrowband than with broadband ultraviolet B phototherapy. Photodermatol Photoimmunol Photomed 2009;25:119-23.
13. Czarnecki D. Narrowband ultraviolet B therapy is an effective means of raising serum vitamin D levels. Clin Exp Dermatol 2008;33:202.
14. Osmancevic A, Landin-Wilhelmsen K, Larko O , Krogstad AL. Vitamin D status in psoriasis patients during different treatments with phototherapy. J Photochem Photobiol B 2010;101:117-23.

15. Lesiak A, Narbutt J, Pawlaczyk M, Sysa-Jedrzejowska A , Krzyscin J. Vitamin D serum level changes in psoriatic patients treated with narrowband ultraviolet B phototherapy are related to the season of the irradiation. Photodermatol Photoimmunol Photomed 2011;27:304-10.
16. Rogers S, Marks J, Shuster S , Hillyard CJ. Effect of PUVA on serum 25-OH vitamin D in psoriatics. Br Med J 1979;2:833-4.
17. Bogh MK, Schmedes AV, Philipsen PA, Thieden E , Wulf HC. Vitamin D production after UVB exposure depends on baseline vitamin D and total cholesterol but not on skin pigmentation. J Invest Dermatol 2010;130:546-53.
18. Bogh MK, Schmedes AV, Philipsen PA, Thieden E , Wulf HC. Vitamin D production depends on ultraviolet-B dose but not on dose rate: a randomized controlled trial. Exp Dermatol 2011;20:14-8.
19. Olds WJ, McKinley AR, Moore MR , Kimlin MG. In vitro model of vitamin D3 (cholecalciferol) synthesis by UV radiation: dose-response relationships. J Photochem Photobiol B 2008;93:88-93.
20. Webb AR, DeCosta BR , Holick MF. Sunlight regulates the cutaneous production of vitamin D3 by causing its photodegradation. J Clin Endocrinol Metab 1989;68:882-7.
21. Krause R, Buhring M, Hopfenmuller W, Holick MF , Sharma AM. Ultraviolet B and blood pressure. Lancet 1998;352:709-10.
22. MacLaughlin J , Holick MF. Aging decreases the capacity of human skin to produce vitamin D3. J Clin Invest 1985;76:1536-8.
23. Bogh MK, Schmedes AV, Philipsen PA, Thieden E , Wulf HC. Interdependence between body surface area and ultraviolet B dose in vitamin D production: a randomized controlled trial. Br J Dermatol 2011;164:163-9.
24. Barysch MJ, Hofbauer GF , Dummer R. Vitamin D, ultraviolet exposure, and skin cancer in the elderly. Gerontology 2010;56:410-3.
25. Barysch MJ, Feldmeyer L, Bischoff-Ferrari H, Hofbauer G , Dummer R. [Vitamin D, ultraviolet rays and skin cancer]. Rev Med Suisse 2010;6:884-5.

Table legends

Table 1

Multivariate analysis for change in vitamin D serum level between beginning and end of therapy

Table 2

Serum concentrations of vitamin D before and after 12-week UV therapy

Table 3

Diagnosis and phototherapy

Table 1: Multivariate analysis for change in vitamin D serum level between beginning and end of therapy

Univariate analysis (adjusted for therapy)	**Change in vit D level**	**Multiple linear regression R^2(adj)=0.582**		
		beta	**p**	**95% CI**
age	p = 0.905			
gender	*p = 0.033*	7.2	0.02	1.1; 13.2
BMI	p = 0.85			
blood pressure	p = 0.208			
UVA1 therapy	*p <0.001*	-17.457	<0.001	-24.013; -10.901
UVA/UVBnb therapy		11.144		3.789; 18.498
UVBnb therapy				
season	*p = 0.012*	12.3 (0,0) 0 7.5 (0,1) 1 4.1 (1,0) 2 baseline (1,1) 3	0.028	3.945; 20.579 0.111; 14.903 -3.197; 11,469
diagnosis *(4=baseline)*	p = 0.634			
calcium	p = 0.098			
phosphate	p = 0.124			
log (CRP)	p = 0.651			

PTH/ change in PTH	p = 0.596/ p = 0.433			

Table 2: Serum concentrations of vitamin D before and after 12-week UV therapy

	At onset mean (median) [ng/ml]	After treatment mean (median) [ng/ml]	Change in serum [ng/ml]	p-value
25(OH)D after UVBnb	22.058 +/- 10.3 (21.900)	39.467 +/- 12.2 (38.300)	18.6 +/- 4.6	p<0.001
25(OH)D after UVA/UVBnb	23.917 +/- 20.2 (20.050)	50.278 +/- 22.9 (44.750)	29.7 +/- 3.7	p=0.003
25(OH)D after UVA1	21.900 +/- 9.7 (21.400)	18.984 +/- 8.3 (18.600)	- 1.1 + /- 3.3	p<0.001

Table 3: Diagnosis and phototherapy

Therapy	Diagnosis (number of cases*)
UVA1	Morphoea (13), scleroderma (4), lichen sclerosus et atrophicus, atrophoderma idiopathica et progressive, cutaneous verrucous lupus erythematodes, melanosis circumscripta, oid-oid, telangiectasia macularis eruptiva perstans, melanosis circumscripta
UVA/UVBnb	Atopic dermatitis (16), other eczems (6), prurigo simplex subacuta (3), lichen planus
UVBnb	Psoriasis (25), vitiligo (5), mycosis fungoides (2), Mallorca acne

*When number of cases not indicated: unique case.

Figure legends

Figure 1

Patient flow chart

Figure 2a

Vitamin D change after 2 weeks phototherapy

Figure 2b

Vitamin D change after 12 weeks phototherapy

Figure 1: Patient flow chart

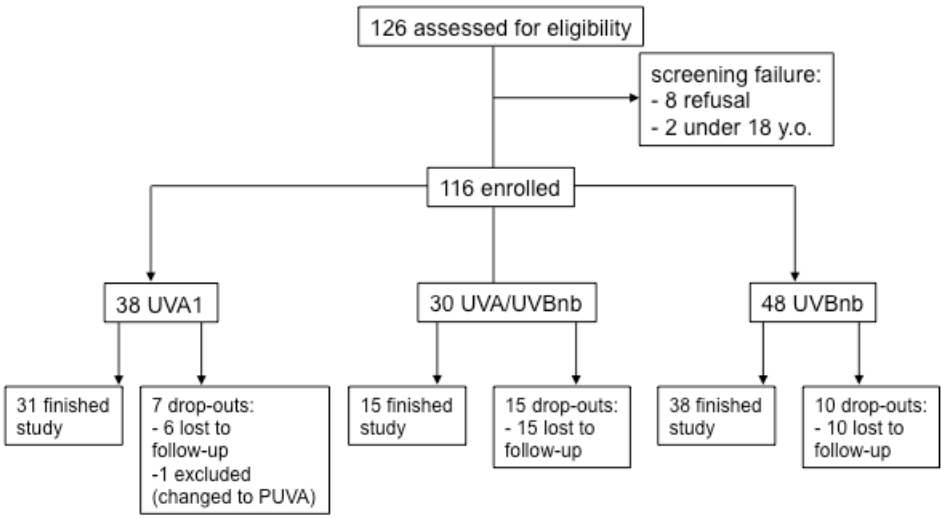

Figure 2a: Vitamin D change after 2 weeks phototherapy

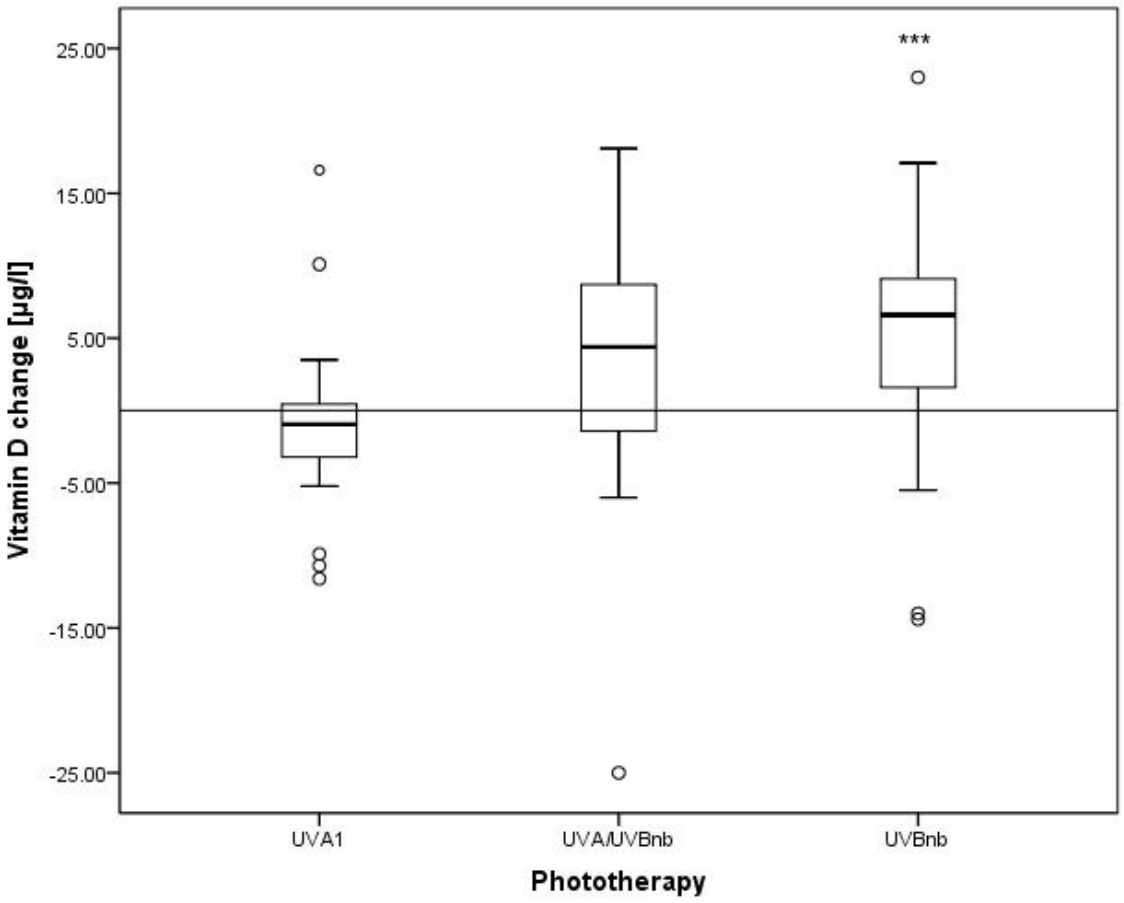

Figure 2b: Vitamin D change after 12 weeks phototherapy